

CLAIMS

what is claimed is:

1. A method of evaluating the effect of interactions between distinct cell types,
5 the method comprising:

(a) providing a first cell culture of a first cell type and a second cell culture of a
second cell type in a microenvironment in which the cells of the first and second cell
cultures share a common medium, and wherein the first and second cell types interact in the
common medium;

10 (b) imaging the first and second cell types after exposure to an agent or stimulus;
and

(c) quantitatively evaluating one or more images obtained in (b) to identify any
effects of the agent on quantitative representations of the phenotypes of the cells in the first
and second cell cultures, which effects are mediated by interactions between the first and
15 second cell cultures.

2. The method of claim 1, wherein quantitatively evaluating one or more images
identifies at least one of a change in migration pattern, growth rate, endocytosis, cell shape,
and extracellular matrix deposition of the cells of at least one of the first and second cell
20 cultures.

3. The method of claim 1, wherein the agent is a chemical compound or a
biological material

25 4. The method of claim 1, wherein the agent is a drug candidate.

5. The method of claim 1, wherein the agent is electromagnetic radiation,
particle radiation, a non-ambient temperature, a non-ambient pressure, acoustic energy, a
mechanical force, an electrical field, a magnetic field, and combinations thereof.

30 6. The method of claim 1, wherein the biological condition is a disease.

7. The method of claim 6, wherein the biological condition is a cancer, Type I
diabetes, Type II diabetes, a neurodegenerative disease, a cardiovascular disease, vascular
35 disease or an auto-immune disease.

8. The method of claim 1, wherein the biological condition is normal
unperturbed functioning of an organ or tissue and the agent causes one or more of the cell
types to become abnormal.

40 9. The method of claim 1, wherein the biological condition is a cancer,
wherein the first cell type is a cancerous epithelial cell type and the second cell type
is a mesenchymal cell type, and
wherein the first and second cell types are from the same tissue or organ.

45 10. The method of claim 1, wherein the biological condition is a cancer,

wherein the first cell type is a cancerous epithelial cell type and the second cell type is an endothelial cell type, and

wherein the first and second cell types are from the same tissue or organ.

5 11. The method of claim 1, wherein the biological condition is a cancer and wherein the first cell type is a cancerous cell type and the second cell type is an immune system cell type.

10 12. The method of claim 1, wherein the biological condition is an auto-immune disease, and wherein the first cell type is an immune system cell type and the second cell type is a different cell type that is attacked by cells of the first cell type in the auto-immune disease.

15 13. The method of claim 1, wherein the biological condition is a neuro-degenerative disease, and wherein the first cell type is a neuron cell type and the second cell type is a neuroglial cell type.

20 14. The method of claim 13, wherein the biological condition is Parkinson's disease, and wherein the first cell type is a neuron cell type and the second cell type is an astrocyte cell type, oligodendrocyte cell type, immune system cell type, or a vascular cell type.

25 15. The method of claim 13, wherein the biological condition is Alzheimer's disease, and wherein the first cell type is a cholinergic neuron cell type and the second cell type is a neuroglial cell type.

30 16. The method of claim 1, wherein the biological condition is Type II diabetes, and wherein the first cell type is a muscle cell type and the second cell type is an adipocyte cell type, an immune cell type, or a vascular cell type.

 17. The method of claim 1, wherein the biological condition is cardiac disease, and wherein the first cell type is a cardiac myocyte and the second cell type is a stem cell, primary cell, fibroblast or endothelial cell of cardiac origin.

35 18. The method of claim 1, wherein identifying any effects of the agents comprises determining a cell killing potency of the agent.

40 19. The method of claim 18, wherein the biological condition is a cancer, wherein the first cell type is a cancerous epithelial cell type and the second cell type is a mesenchymal cell type,
 wherein the first and second cell types are from the same tissue or organ, and
 wherein the agent is predicted to be effective against cancer when the one or more images show that it has an EC50 for the cancerous epithelial cells that is substantially greater than the EC50 for the mesenchymal cells.

45 20. The method of claim 1, wherein the common medium is a cell growth medium or a cell support medium.

21. The method of claim 1, further comprising:
prior to imaging, allowing the cells of the first and second cell types to grow
in the common growth medium.

5 22. The method of claim 1, wherein the microenvironment comprises:
a first compartment in which the first cell culture is grown, and
a second compartment in which the second cell culture is grown, and
wherein the common medium contacts the first and second compartments and
the first and second cell cultures.

10 23. The method of claim 22, wherein the first compartment is a base
compartment holding the first cell culture at first level,
wherein the second compartment is provided as an insert to the base
compartment, and
15 wherein the second compartment holds the second cell culture at a second
level, that is above the first level.

24. A method of evaluating the effect of an agent on a biological condition, the
method comprising:

20 (a) providing a first cell culture of cells of a first cell type and a second cell
culture of cells of a second cell type in a microenvironment in which the cells of first and
second cell cultures share a common medium, wherein the first and second cell types interact
as part of the biological condition;

(b) exposing the cells of the microenvironment to the agent;

25 (c) imaging the first and second cell types after exposure to the agent; and

(d) quantitatively evaluating one or more images obtained in (c) to determine
how the agent affects quantitative representations of phenotypes of the cells, thereby
predicting the effect of the agent in treating the biological condition.

30 25. The method of claim 24, wherein quantitatively evaluating one or more
images identifies at least one of a change in migration pattern, growth rate, endocytosis, cell
shape, and extracellular matrix deposition of the cells of at least one of the first and second
cell cultures.

35 26. The method of claim 24, wherein the agent is a drug candidate.

27. The method of claim 24, wherein the biological condition is a disease.

40 28. The method of claim 24, wherein the biological condition is normal
unperturbed functioning of an organ or tissue and the agent causes one or more of the cell
types to become abnormal.

29. The method of claim 24, wherein the common medium is a cell growth
medium or a cell support medium.

45 30. The method of claim 24, wherein the microenvironment comprises:
a first compartment in which the first cell culture is grown, and
a second compartment in which the second cell culture is grown, and

wherein the common medium contacts the first and second compartments and the first and second cell cultures.

5 31. A method of evaluating an agent's effect on a biological condition, the method comprising:

- (a) exposing cells of a first cell type and cells of a second cell type to the agent, wherein the first and second cell types interact in producing the biological condition;
- (b) imaging cells of the first and second cell types after exposure to the agent;
- 10 (c) quantitatively evaluating images obtained in (b) to identify any effects of the agent on quantitative representations of phenotypes of the cells of the first and second cell types; and
- (d) based upon any effects identified at (c), predicting the agent's effect on the biological condition.

15 32. The method of claim 31, wherein quantitatively evaluating one or more images obtained in (b) to identify any effects of the agent comprises identifying changes in at least one of the viability, the function, and the morphology of the cells of at least one of the first and second cell types.

20 33. The method of claim 31, wherein quantitatively evaluating one or more images identifies at least one of a change in migration pattern, growth rate, endocytosis, cell shape, and extracellular matrix deposition of the cells of at least one of the first and second cell cultures.

25 34. The method of claim 31, wherein the agent is a chemical compound or a biological material

30 35. The method of claim 31, wherein the agent is electromagnetic radiation, particle radiation, a non-ambient temperature, a non-ambient pressure, acoustic energy, a mechanical force, an electrical field, a magnetic field, and combinations thereof.

36. The method of claim 31, wherein the biological condition is a disease.

35 37. The method of claim 36, wherein the biological condition is a cancer, Type I diabetes, Type II diabetes, a neurodegenerative disease, a cardiovascular disease, or an autoimmune disease.

40 38. The method of claim 31, wherein the biological condition is normal unperturbed functioning of an organ or tissue and the agent causes one or more of the cell types to become abnormal.

45 39. The method of claim 31, wherein the biological condition is a cancer, wherein the first cell type is a cancerous epithelial cell type and the second cell type is a mesenchymal cell type, and wherein the first and second cell types are from the same tissue or organ.

40. The method of claim 31, wherein the biological condition is a cancer,

wherein the first cell type is a cancerous epithelial cell type and the second cell type is an endothelial cell type, and
wherein the first and second cell types are from the same tissue or organ.

5 41. The method of claim 31, wherein the biological condition is a cancer and wherein the first cell type is a cancerous cell type and the second cell type is an immune system cell type.

10 42. The method of claim 31, wherein the biological condition is an auto-immune disease, and wherein the first cell type is an immune system cell type and the second cell type is a different cell type that is attacked by cells of the first cell type in the auto-immune disease.

15 43. The method of claim 31, wherein the biological condition is a neuro-degenerative disease, and wherein the first cell type is a neuron cell type and the second cell type is a neuroglial cell type.

20 44. The method of claim 31, wherein the biological condition is Type II diabetes, and wherein the first cell type is a muscle cell type and the second cell type is an adipocyte cell type, an immune cell type, or a vascular cell type.

25 45. The method of claim 31, wherein the biological condition is cardiac disease, and wherein the first cell type is a cardiac myocyte and the second cell type is a stem cell, primary cell, fibroblast or endothelial cell of cardiac origin.